General

Guideline Title

Final recommendation statement: latent tuberculosis infection: screening.

Bibliographic Source(s)

Final recommendation statement: latent tuberculosis infection: screening. [internet]. Rockville (MD): U.S. Preventive Services Task Force (USPSTF); 2016 Sep [8 p]. [38 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: U.S. Preventive Services Task Force. Guide to clinical preventive services. 2nd ed. Baltimore (MD): Williams & Wilkins; 1996. Chapter 25, Screening for tuberculosis infection - including Bacille Calmette-Guerin immunization. p. 277-86. [55 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The US Preventive Services Task Force (USPSTF) grades its recommendations (A, B, C, D, or I) and identifies the Levels of Certainty regarding Net Benefit (High, Moderate, and Low). The definitions of these grades can be found at the end of the "Major Recommendations" field.

Summary of Recommendation and Evidence

The USPSTF recommends screening for latent tuberculosis infection (LTBI) in populations at increased risk (B recommendation).

Clinical Considerations

Patient Population Under Consideration

This recommendation applies to asymptomatic adults 18 years and older at increased risk for tuberculosis (see the "Assessment of Risk" section for more information). It does not apply to adults with symptoms of tuberculosis or to children and adolescents.

Assessment of Risk

Populations at increased risk for LTBI based on increased prevalence of active disease and increased risk of exposure include persons who were born in, or are former residents of, countries with increased tuberculosis prevalence and persons who live in, or have lived in, high-risk congregate settings (e.g., homeless shelters and correctional facilities). Clinicians can consult their local or state health departments for more information about populations at risk in their community, because local demographic patterns may vary across the United States.

In 2015, among persons of known national origin, 66.2% of all active tuberculosis cases in the U.S. were among foreign-born persons, and the case rate of active tuberculosis among foreign-born persons was approximately 13 times higher than among U.S.-born persons (15.1 vs. 1.2 cases per 100,000 persons). More than half of all foreign-born persons in the U.S. with active tuberculosis were from 5 countries: Mexico, the Philippines, Vietnam, India, and China. In addition, the Centers for Disease Control and Prevention (CDC) has identified foreign-born persons from Haiti and Guatemala as important contributors to active tuberculosis cases in the U.S. The World Health Organization (WHO) recently updated its list of countries with a high burden of tuberculosis to include the top 20 countries with the highest absolute numbers of cases and an additional 10 countries with the most severe burden in terms of case rate per capita.

Persons who live in, or have lived in, high-risk congregate settings also have a higher prevalence rate of active tuberculosis and increased risk for exposure. Among persons 15 years and older with active tuberculosis, 5.6% were homeless within the past year, 2.2% were residents of a long-term care facility, and 4.2% were in a correctional facility at the time of diagnosis. Published prevalence rates of LTBI in these settings vary widely, depending on the type of screening test used, the tuberculin skin test (TST) threshold used to define the presence of LTBI, and the population studied. Estimates of LTBI prevalence range from 23.1% to 87.6% among prisoners and from 18.6% to 79.8% among persons who are homeless.

Other populations at increased risk for LTBI or progression to active disease include persons who are immunosuppressed (e.g., persons living with human immunodeficiency virus [HIV], patients receiving immunosuppressive medications such as chemotherapy or tumor necrosis factor–alpha inhibitors, and patients who have received an organ transplant) and patients with silicosis (a lung disease). However, given that screening in these populations may be considered standard care as part of disease management or indicated prior to the use of certain medications, the USPSTF did not review evidence on screening in these populations. Some evidence from observational studies has explored the association between poorly controlled diabetes and progression of LTBI to active disease. However, there is insufficient evidence on screening for and treatment of LTBI in persons with diabetes for the USPSTF to make a separate recommendation for this important subgroup.

Persons who are contacts of individuals with active tuberculosis, health care workers, and workers in high-risk congregate settings may also be at increased risk of exposure. Because screening in these populations is conducted as part of public health or employee health surveillance, the USPSTF did not review the evidence in these populations. Clinicians seeking further information about testing for tuberculosis in these populations can refer to the "Useful Resources" and "Recommendations of Others" sections.

Screening Tests

Two types of screening tests for LTBI are currently available in the United States: the TST and interferon-gamma release assay (IGRA). The TST requires intradermal placement of purified protein derivative and interpretation of response 48 to 72 hours later. The skin test reaction is measured in millimeters of the induration (a palpable, raised, hardened area or swelling). IGRAs require a single venous blood sample and laboratory processing within 8 to 30 hours after collection. Two types of IGRAs are currently approved by the U.S. Food and Drug Administration: T-SPOT.TB (Oxford Immunotec Global) and QuantiFERON-TB Gold In-Tube (Qiagen).

Numerous patient and systems factors may influence the selection of a screening test. Generally, the CDC recommends screening with either the TST or IGRA but not both. Testing with IGRAs may be

preferable for persons who have received a bacillus Calmette-Guérin (BCG) vaccination or persons who may be unlikely to return for TST interpretation. Additional information on the use and interpretation of the TST and IGRA is available from the CDC.

Screening Intervals

The USPSTF found no evidence on the optimal frequency of screening for LTBI. Depending on specific risk factors, screening frequency could range from 1-time only screening among persons who are at low risk for future tuberculosis exposure to annual screening among those who are at continued risk of exposure.

Treatment

Recommendations for the treatment of LTBI are available from the CDC.

Definitions

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality or conflicting, and the balance of benefits and harms cannot be determined.	Read the "Clinical Considerations" section of USPSTF Recommendation Statement (see the "Major Recommendations" field). If offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as: The number, size, or quality of individual studies Inconsistency of findings across individual studies

Level of Certainty	Description
	Limited generalizability of findings to routine primary care practice Lack of coherence in the chain of evidence
	As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: The limited number or size of studies Important flaws in study design or methods Inconsistency of findings across individual studies Gaps in the chain of evidence Findings not generalizable to routine primary care practice A lack of information on important health outcomes More information may allow an estimation of effects on health outcomes.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Latent tuberculosis infection

Guideline Category

Prevention

Screening

Clinical Specialty

Family Practice

Infectious Diseases

Internal Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To issue a current U.S. Preventive Services Task Force (USPSTF) recommendation on screening for latent tuberculosis infection (LTBI)

Target Population

Asymptomatic adults 18 years and older at increased risk for tuberculosis

Note: The guideline does not apply to adults with symptoms of tuberculosis or to children and adolescents.

Interventions and Practices Considered

Screening for latent tuberculosis infection (tuberculin skin test [TST] or interferon-gamma release assay [IGRA])

Major Outcomes Considered

- Key Question 1: Is there direct evidence that targeted screening for latent tuberculosis infection (LTBI) in primary care settings in asymptomatic adults at increased risk for developing active tuberculosis disease (e.g., individuals in populations with a high prevalence of active TB disease or with documented increased risk for progression from LTBI to active TB disease) improves quality of life, or reduces active TB disease incidence, or reduces transmission of TB, or reduces disease-specific or overall mortality?
- Key Question 2:
  a. What is the accuracy and reliability of the tuberculin skin test (TST) or the interferon-gamma release assay (IGRA) for screening asymptomatic adults who are at increased risk for developing active TB disease?
  b. What is the accuracy and reliability of sequential screening strategies that include both TST and IGRA testing in asymptomatic adults who are at increased risk for developing active TB disease?
- Key Question 3: Does treatment of LTBI with the Centers for Disease Control and Prevention (CDC)-recommended pharmacotherapy regimens improve quality of life or reduce progression to active TB disease, or reduce transmission of TB, or reduce disease-specific or overall mortality?
- Key Question 4: Are there harms associated with screening for LTBI?
  a. Do these harms differ by screening method or strategy?
  b. Do these harms differ by population?
- Key Question 5: Are there harms associated with treatment for LTBI with CDC-recommended pharmacotherapy regimens?

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by the RTI International–University of North Carolina Evidence-based Practice Center (EPC) for the U.S. Preventive Services Task Force (USPSTF) (see the "Availability of Companion Documents" field).

Data Sources and Searches

PubMed/MEDLINE and the Cochrane Library were searched for English-language articles published from database inception through August 3, 2015. The search strategies for these databases are listed in the eMethods in the systematic review supplement. ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform were also searched for unpublished literature. To supplement electronic searches, the reference lists of pertinent articles and all studies suggested by reviewers or comments received during public commenting periods were reviewed. Since August 2015, ongoing surveillance has been conducted through article alerts and targeted searches of high-impact journals to identify major studies published in the interim that may affect the conclusions or understanding of the evidence and therefore the related USPSTF recommendation. The last surveillance was conducted on May 31, 2016, and no new studies were identified.

Study Selection

Two investigators independently reviewed titles, abstracts, and full-text articles using prespecified inclusion criteria for each key question (KQ) (see eTable 2 in the systematic review supplement). Disagreements about inclusion were resolved by discussion. Only studies rated as of fair or good quality were included. For the overarching question regarding direct evidence of benefits of screening (KQ1), only randomized controlled trials (RCTs) or prospective cohort studies that compared screening with no screening in primary care settings and focused on asymptomatic adults belonging to populations at increased risk for developing active tuberculosis (TB) were eligible. Primary care was broadly defined to include public health settings or specialized clinics providing primary care functions (e.g., prison clinics). Studies in which more than 25% of the study population were younger than 18 years or were known to be human immunodeficiency virus (HIV) positive were excluded, unless results were stratified by these characteristics. Studies on close contacts of individuals with active TB were excluded because testing and treatment of such populations is considered a public health surveillance activity. Studies of individuals with underlying immunosuppression and for whom latent tuberculosis infection (LTBI) screening and treatment would be part of disease management were also excluded, for example, studies of individuals beginning treatment with tumor necrosis factor–alpha inhibitors. Other populations at increased risk were included, such as persons who had previously received the bacillus Calmette–Guérin (BCG) vaccination, injection drug users, persons who were homeless or residing in homeless shelters, former prisoners, persons born in or former residents of countries with high TB prevalence, persons who worked with such individuals, and persons with a documented increased risk for progression from LTBI to active TB.

For screening test accuracy and reliability (KQ2), studies assessing the tuberculin skin test (TST) using the Mantoux method and 3 interferon-gamma release assays (IGRAs) were included. Because there is no direct reference test for latent infection, the reviewers relied on studies of individuals with bacteriologically confirmed active TB conducted in any country or setting for sensitivity and on studies of healthy participants at low risk for TB and TB exposure that were conducted in countries not considered as having high TB burden for specificity. Reliability was defined as the degree to which a test provided stable and consistent results, including outcomes such as test-retest reliability, inter-rater reliability, and inter-laboratory reliability.

To review the benefits (KQ3) and harms (KQ5) of treatment, RCTs of individuals with LTBI that compared a Centers for Disease Control and Prevention (CDC)-recommended treatment (medication, dose, and duration) with placebo, delayed treatment, no treatment, or another CDC-recommended treatment were included. For harms of treatment (KQ5), prospective cohort studies and case-control studies were also eligible. For harms associated with screening (KQ4), systematic reviews, RCTs, and prospective cohort studies reporting false-positive results leading to unnecessary testing (e.g., chest radiography) or treatment, labeling, stigma, anxiety, or cellulitis were eligible.

Except for studies of screening test accuracy and reliability (KQ2), studies conducted in countries

categorized as anything other than "very high" on the United Nations Human Development Index were excluded.

Number of Source Documents

See the literature flow diagram (Figure 2) in the systematic review (see the "Availability of Companion Documents" field) for a summary of evidence search and selection.

Articles included for Key Questions:

- Key Question 1: 0 studies
- Key Question 2: 67 studies
- Key Question 3: 3 studies
- Key Question 4: 0 studies
- Key Question 5: 5 studies

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Two independent investigators assessed the quality of each study as good, fair, or poor, using predefined criteria developed by the U.S. Preventive Services Task Force (USPSTF) and adapted for this topic (see eTable 3 in the systematic review supplement [see the "Availability of Companion Documents" field]).

Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review and full report were prepared by the RTI International–University of North Carolina Evidence-based Practice Center (EPC) for the U.S. Preventive Services Task Force (USPSTF) (see the "Availability of Companion Documents" field).

Data Extraction and Quality Assessment

For each included study, one investigator extracted information about design, population, tests or treatments used, and outcomes (e.g., sensitivity, specificity, active tuberculosis [TB]), and a second investigator reviewed for completeness and accuracy. Two independent investigators assessed the quality of each study as good, fair, or poor, using predefined criteria developed by the USPSTF and adapted for this topic (see eTable 3 in the systematic review supplement). Individual study quality ratings are provided in eTables 4-7 in the systematic review supplement.

Data Synthesis and Analysis

Findings for each question are summarized in tabular and narrative form. To determine whether meta-analyses were appropriate, the number of studies available and the clinical and methodological heterogeneity of the studies following established guidance were assessed. To do this, the populations,

similarities and differences in screening tests or treatments used, and similarities in outcomes and timing of measured outcomes, were qualitatively assessed. When at least 3 similar studies were available, quantitative synthesis was conducted with random-effects models using the inverse variance weighted method (DerSimonian and Laird) to determine pooled estimates. Statistical heterogeneity was assessed using the I^2 statistic. Results for benefits and harms of treatment (Key Question [KQ] 3 and KQ5) were considered statistically significant if the *P* value was less than .05 based on 2-sided testing. All quantitative analyses were conducted using Stata version 13.1 (StataCorp).

Sensitivity analyses for screening test accuracy (KQ2) added in 19 studies rated as poor quality to determine whether inclusion of such studies would have altered conclusions. For benefits (KQ3) and harms (KQ5) of treatment, sensitivity analyses also added 6 randomized controlled trials (RCTs) comparing isoniazid with placebo that were either poor quality, did not meet all of the inclusion criteria, or both, because they used a longer duration of treatment than is currently recommended (e.g., they used 1 year of isoniazid or 3 months of isoniazid); some also used lower or higher doses than currently recommended. For RCTs to be included in sensitivity analyses, they either confirmed latent tuberculosis infection (LTBI) for participants to be eligible (e.g., by enrolling only those who were tuberculin skin test [TST] positive), reported data for those with confirmed LTBI (e.g., for the TST-positive subset of participants), or the vast majority of participants (more than 75%) were TST positive.

For all quantitative syntheses, sensitivity analyses were conducted using maximum likelihood random-effects (KQ2) or profile likelihood random-effects methods (KQs 3 and 5) because DerSimonian and Laird models may not perform well when few studies are included. Results were essentially the same as for those using DerSimonian and Laird random-effects models, with some minor variation in width of confidence intervals for some estimates, and thus are not reported further.

Methods Used to Formulate the Recommendations

Balance Sheets

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The U.S. Preventive Services Task Force (USPSTF) systematically reviews the evidence concerning both the benefits and harms of widespread implementation of a preventive service. It then assesses the certainty of the evidence and the magnitude of the benefits and harms. On the basis of this assessment, the USPSTF assigns a letter grade to each preventive service signifying its recommendation about provision of the service (see table below). An important, but often challenging, step is determining the balance between benefits and harms to estimate "net benefit" (that is, benefits minus harms).

U.S. Preventive Services Task Force Recommendation Grid*

Certainty of Net Benefit	**Magnitude of Net Benefit**			
	Substantial	**Moderate**	**Small**	**Zero/Negative**
High	A	B	C	D
Moderate	B	B	C	D
Low	Insufficient			

**A*, *B*, *C*, *D*, and *I (Insufficient)* represent the letter grades of recommendation or statement of insufficient evidence assigned by the USPSTF after assessing certainty and magnitude of net benefit of the service (see the "Rating Scheme for the Strength of the Recommendations" field).

The overarching question that the USPSTF seeks to answer for every preventive service is whether evidence suggests that provision of the service would improve health outcomes if implemented in a

general primary care population. For screening topics, this standard could be met by a large randomized controlled trial (RCT) in a representative asymptomatic population with follow-up of all members of both the group "invited for screening" and the group "not invited for screening."

Direct RCT evidence about screening is often unavailable, so the USPSTF considers indirect evidence. To guide its selection of indirect evidence, the Task Force constructs a "chain of evidence" within an analytic framework. For each key question, the body of pertinent literature is critically appraised, focusing on the following 6 questions:

Do the studies have the appropriate research design to answer the key question(s)?
To what extent are the existing studies of high quality? (i.e., what is the internal validity?)
To what extent are the results of the studies generalizable to the general U.S. primary care population and situation? (i.e., what is the external validity?)
How many studies have been conducted that address the key question(s)? How large are the studies? (i.e., what is the precision of the evidence?)
How consistent are the results of the studies?
Are there additional factors that assist the USPSTF in drawing conclusions (e.g., presence or absence of dose–response effects, fit within a biologic model)?

The next step in the USPSTF process is to use the evidence from the key questions to assess whether there would be net benefit if the service were implemented. In 2001, the USPSTF published an article that documented its systematic processes of evidence evaluation and recommendation development. At that time, the USPSTF's overall assessment of evidence was described as good, fair, or poor. The USPSTF realized that this rating seemed to apply only to how well studies were conducted and did not fully capture all of the issues that go into an overall assessment of the evidence about net benefit. To avoid confusion, the USPSTF has changed its terminology. Whereas individual study quality will continue to be characterized as good, fair, or poor, the term *certainty* will now be used to describe the USPSTF's assessment of the overall body of evidence about net benefit of a preventive service and the likelihood that the assessment is correct. Certainty will be determined by considering all 6 questions listed above; the judgment about certainty will be described as high, moderate, or low.

In making its assessment of certainty about net benefit, the evaluation of the evidence from each key question plays a primary role. It is important to note that the USPSTF makes recommendations for real-world medical practice in the United States and must determine to what extent the evidence for each key question—even evidence from screening RCTs or treatment RCTs—can be applied to the general primary care population. Frequently, studies are conducted in highly selected populations under special conditions. The USPSTF must consider differences between the general primary care population and the populations studied in RCTs and make judgments about the likelihood of observing the same effect in actual practice.

It is also important to note that one of the key questions in the analytic framework refers to the potential harms of the preventive service. The USPSTF considers the evidence about the benefits and harms of preventive services separately and equally. Data about harms are often obtained from observational studies because harms observed in RCTs may not be representative of those found in usual practice and because some harms are not completely measured and reported in RCTs.

Putting the body of evidence for all key questions together as a chain, the USPSTF assesses the certainty of net benefit of a preventive service by asking the 6 major questions listed above. The USPSTF would rate a body of convincing evidence about the benefits of a service that, for example, derives from several RCTs of screening in which the estimate of benefits can be generalized to the general primary care population as "high" certainty (see the "Rating Scheme for the Strength of Recommendations" field). The USPSTF would rate a body of evidence that was not clearly applicable to general practice or has other defects in quality, research design, or consistency of studies as "moderate" certainty. Certainty is "low" when, for example, there are gaps in the evidence linking parts of the analytic framework, when evidence to determine the harms of treatment is unavailable, or when evidence about the benefits of treatment is insufficient. Table 4 in the methodology document listed below (see the "Availability of Companion

Documents" field) summarizes the current terminology used by the USPSTF to describe the critical assessment of evidence at all 3 levels: individual studies, key questions, and overall certainty of net benefit of the preventive service.

Sawaya GF, Guirguis-Blake J, LeFevre M, Harris R, Petitti D; U.S. Preventive Services Task Force. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. Ann Intern Med. 2007;147:871-875. [5 references].

Rating Scheme for the Strength of the Recommendations

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality or conflicting, and the balance of benefits and harms cannot be determined.	Read the "Clinical Considerations" section of the USPSTF Recommendation Statement (see the "Major Recommendations" field). If offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as: The number, size, or quality of individual studies Inconsistency of findings across individual studies Limited generalizability of findings to routine primary care practice Lack of coherence in the chain of evidence As more information becomes available, the magnitude or direction of the observed effect

Level of Certainty	Description
	could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: The limited number or size of studies Important flaws in study design or methods Inconsistency of findings across individual studies Gaps in the chain of evidence Findings not generalizable to routine primary care practice A lack of information on important health outcomes More information may allow an estimation of effects on health outcomes.

Cost Analysis

The U.S. Preventive Services Task Force (USPSTF) does not consider the costs of providing a service in this assessment.

Method of Guideline Validation

Comparison with Guidelines from Other Groups

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Peer Review

Before the U.S. Preventive Services Task Force (USPSTF) makes its final determinations about recommendations on a given preventive service, the Evidence-based Practice Center (EPC) and the Agency for Healthcare Research and Quality (AHRQ) send the draft evidence review to 4 to 6 external experts and to Federal agencies and professional and disease-based health organizations with interests in the topic. The experts are asked to examine the review critically for accuracy and completeness and to respond to a series of specific questions about the document. The draft evidence review is also posted on the USPSTF Web site for public comment. After assembling these external review comments and documenting the proposed response to key comments, the topic team presents this information to the USPSTF in memo form. In this way, the USPSTF can consider these external comments before it votes on its recommendations about the service. Draft recommendation statements are then circulated for comment among reviewers representing professional societies, voluntary organizations, and Federal agencies, as well as posted on the USPSTF Web site for public comment. These comments are discussed before the final recommendations are confirmed.

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from March 8 to April 4, 2016. Many comments sought clarification around risk assessment of populations who should receive screening. The USPSTF clarified that given regional variations in the local populations considered at risk for tuberculosis, clinicians may consult their local or state public health agency for additional details on specific populations at risk in their community. Furthermore, the USPSTF clarified that although persons with diabetes and pregnant women are not addressed separately in this recommendation statement, they are also not excluded from the recommendation. A few public comments sought clarification on the recommended frequency of screening. Although the USPSTF sought evidence on screening frequency, there was not enough evidence available to determine an optimal screening interval. Several comments requested that the recommendation include treatment of latent tuberculosis infection (LTBI). While the USPSTF acknowledges that treatment of LTBI contributes to the success of LTBI

screening, it is beyond the scope of the USPSTF to make any specific recommendations on treatment. The Centers for Disease Control and Prevention (CDC) provides treatment guidelines for LTBI.

Comparison with Guidelines from Other Groups

Recommendations for screening from the following groups were discussed: the American Academy of Family Physicians, the CDC, the American Thoracic Society, the Infectious Diseases Society of America, and the World Health Organization (WHO).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is not specifically stated for each recommendation.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Benefits of Early Detection and Treatment

The U.S. Preventive Services Task Force (USPSTF) found no studies that evaluated the direct benefits of screening for latent tuberculosis infection (LTBI). The USPSTF found adequate evidence that treatment of LTBI with regimens recommended by the Centers for Disease Control and Prevention (CDC) decreases progression to active tuberculosis; the magnitude of this benefit is moderate.

Potential Harms

Harms of Early Detection and Treatment

The U.S. Preventive Services Task Force (USPSTF) found no direct evidence on the harms of screening for latent tuberculosis infection (LTBI). The USPSTF found adequate evidence that the magnitude of harms of treatment of LTBI with the Centers for Disease Control and Prevention (CDC)-recommended regimens is small. The primary harm of treatment is hepatotoxicity.

Qualifying Statements

Qualifying Statements

- The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific clinical preventive services for patients without obvious related signs or symptoms.
- It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.
- The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

- Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality (AHRQ) or the U.S. Department of Health and Human Services.

Implementation of the Guideline

Description of Implementation Strategy

The experiences of the first and second U.S. Preventive Services Task Force (USPSTF), as well as that of other evidence-based guideline efforts, have highlighted the importance of identifying effective ways to implement clinical recommendations. Practice guidelines are relatively weak tools for changing clinical practice when used in isolation. To effect change, guidelines must be coupled with strategies to improve their acceptance and feasibility. Such strategies include enlisting the support of local opinion leaders, using reminder systems for clinicians and patients, adopting standing orders, and audit and feedback of information to clinicians about their compliance with recommended practice.

In the case of preventive services guidelines, implementation needs to go beyond traditional dissemination and promotion efforts to recognize the added patient and clinician barriers that affect preventive care. These include clinicians' ambivalence about whether preventive medicine is part of their job, the psychological and practical challenges that patients face in changing behaviors, lack of access to health care or of insurance coverage for preventive services for some patients, competing pressures within the context of shorter office visits, and the lack of organized systems in most practices to ensure the delivery of recommended preventive care.

Dissemination strategies have changed dramatically in this age of electronic information. While recognizing the continuing value of journals and other print formats for dissemination, the USPSTF will make all its products available through its Web site . The combination of electronic access and extensive material in the public domain should make it easier for a broad audience of users to access USPSTF materials and adapt them for their local needs. Online access to USPSTF products also opens up new possibilities for the appearance of the annual, pocket-size *Guide to Clinical Preventive Services*.

To be successful, approaches for implementing prevention have to be tailored to the local level and deal with the specific barriers at a given site, typically requiring the redesign of systems of care. Such a systems approach to prevention has had notable success in established staff-model health maintenance organizations, by addressing organization of care, emphasizing a philosophy of prevention, and altering the training and incentives for clinicians. Staff-model plans also benefit from integrated information systems that can track the use of needed services and generate automatic reminders aimed at patients and clinicians, some of the most consistently successful interventions. Information systems remain a major challenge for individual clinicians' offices, however, as well as for looser affiliations of practices in network-model managed care and independent practice associations, where data on patient visits, referrals, and test results are not always centralized.

Implementation Tools

Mobile Device Resources

Patient Resources

Pocket Guide/Reference Cards

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources*

fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Final recommendation statement: latent tuberculosis infection: screening. [internet]. Rockville (MD): U.S. Preventive Services Task Force (USPSTF); 2016 Sep [8 p]. [38 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Sep

Guideline Developer(s)

U.S. Preventive Services Task Force - Independent Expert Panel

Guideline Developer Comment

The U.S. Preventive Services Task Force (USPSTF) is a federally-appointed panel of independent experts. Conclusions of the USPSTF do not necessarily reflect policy of the U.S. Department of Health and Human Services or its agencies.

Source(s) of Funding

The U.S. Preventive Services Task Force (USPSTF) is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality (AHRQ) support the operations of the USPSTF.

Guideline Committee

U.S. Preventive Services Task Force

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*Members of the Task Force at the time this recommendation was finalized. For a list of current Task Force members, go to https://www.uspreventiveservicestaskforce.org/Page/Name/our-members.

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The U.S. Preventive Services Task Force (USPSTF) has an explicit policy concerning conflict of interest. All members disclose at each meeting if they have a significant financial, professional/business, or intellectual conflict for each topic being discussed. USPSTF members with conflicts may be recused from discussing or voting on recommendations about the topic in question.

Disclosures

All authors have completed and submitted the International Committee of Medical Journal Editors (ICMJE) Form for Disclosure of Potential Conflicts of Interest and none were reported. Authors followed the policy regarding conflicts of interest described at https://www.uspreventiveservicestaskforce.org/Page/Name/conflict-of-interest-disclosures. All members of the USPSTF receive travel reimbursement and an honorarium for participating in USPSTF meetings.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: U.S. Preventive Services Task Force. Guide to clinical preventive services. 2nd ed. Baltimore (MD): Williams & Wilkins; 1996. Chapter 25, Screening for tuberculosis infection - including Bacille Calmette-Guerin immunization. p. 277-86. [55 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the U.S. Preventive Services Task Force (USPSTF) Web site.

Availability of Companion Documents

The following are available:

Evidence Reviews:

> Kahwati LC, Feltner C, Halpern M, Woodell CL, Boland E, Amick HR, Palmieri Weber R, Jonas DE. Primary care screening and treatment for latent tuberculosis infection in adults: evidence report and systematic review for the U.S. Preventive Services Task Force. JAMA. 2016 Sep 6;316(9):970-83.
> Kahwati LC, Feltner C, Halpern M, Woodell CL, Boland E, Amick HR, Palmieri Weber R, Jonas DE. Screening for latent tuberculosis infection in adults: an evidence review for the U.S. Preventive Services Task Force. Evidence Synthesis No. 142. Publication No. 14-05212-EF-1. Rockville (MD): Agency for Healthcare Research and Quality; 2016 Sep. 212 p.

Available from the U.S. Preventive Services Task Force (USPSTF) Web site .

Background Articles:

> Barton MB et al. How to read the new recommendation statement: methods update from the U.S. Preventive Services Task Force. Ann Intern Med. 2007;147:123-7.
> Guirguis-Blake J et al. Current processes of the U.S. Preventive Services Task Force: refining evidence-based recommendation development. Ann Intern Med. 2007;147:117-22.
> Sawaya GF et al. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. Ann Intern Med. 2007;147:871-5.

Available from the USPSTF Web site .

The following are also available:

> Screening for latent tuberculosis infection in adults: clinical summary. Rockville (MD): U.S. Preventive Services Task Force; 2016 Sep. 1 p. Available from the USPSTF Web site .

The Electronic Preventive Services Selector (ePSS) is an application designed to provide primary care clinicians and health care teams timely decision support regarding appropriate screening, counseling, and preventive services for their patients. It is based on the current, evidence-based recommendations of the USPSTF and can be searched by specific patient characteristics, such as age, sex, and selected behavioral risk factors.

Patient Resources

The following are available:

> Screening for latent tuberculosis. JAMA patient page. 2016 Sep 6;316(9):1004.

Myhealthfinder is a tool that provides personalized recommendations for clinical preventive services specific to the user's age, gender, and pregnancy status. It features evidence-based recommendations from the U.S. Preventive Services Task Force (USPSTF) and is available at www.healthfinder.gov .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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